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Physiological Event Prediction in Evaluations of Underwater Breathing Apparatus

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14. ABSTRACT. This report describes the use of *Predict*, in-house designed prediction software. NEDU performance goals for underwater breathing apparatus (UBA) based on ventilatory flow rate have served the Navy well for decades. Nevertheless, gas density is a major determinant of respiratory loading at depth, based on both experimental evidence and simple models of fluid mechanics. An understanding of the influence of flow rate and gas density are vital to understanding the performance characteristics of UBA, and the probable tolerance of a diver to those influences. Over a decade ago NEDU developed a constant respiratory impedance model for determining acceptable pressure drops across UBA, and created software to predict the tolerance of divers to UBA under varying dive conditions. The so-called maximum respiratory impedance model was calibrated on Navy manned dive results, and this paper describes the use of that model and the associated *Predict* software to predict diver tolerance based on unmanned data. It is arguably a more complete approach compared to methods already in Navy use, and is particularly useful in estimating the risk of diving UBA made inadequate by design or accident.

15. SUBJECT TERMS
Software, unmanned evaluation, modeling, UBA, diving life support, performance goals, performance limits, fluid dynamics, gas density, respiratory effort, respiratory resistance, respiratory impedance, diving history

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INTRODUCTION

Figure 1. KM 97 helmet on a Navy diver.

One of the functions of the U.S. Navy Experimental Diving Unit (NEDU) is to determine whether diving equipment is safe for use by Navy divers, and whether it is fit for purpose. In other words, does it meet manufacturers' claims, and will it safely support a Navy diver's life-support needs?

The evaluation of diving life support equipment at NEDU begins with a breathing machine testing the equipment in an unmanned testing laboratory in accordance with NEDU's unmanned testing manual[1]. Once test data has been acquired, engineers interpret that data to decide if the equipment is safe for manned diving.

NEDU performance goals based on diver respiratory flow rate have served the Navy well for decades[2,3]. Nevertheless, those historical goals have never explicitly considered gas density, which is a major contributor to the load on a diver's respiratory muscles[4].

An understanding of the influence of both respiratory flow rates and gas density are vital to understanding the complete performance of Underwater Breathing Apparatus (UBA), and the probable tolerance of a diver to that performance. To that end, NEDU developed a constant respiratory impedance approach for determining acceptable pressure drops across UBA[5]. Such an approach serves to combine the best of previous standards for UBA into a unified concept that takes into account engineering principles, psychophysics, and respiratory physiology, including the fluid dynamics of flow in divers' airways.

What is currently illustrated in Technical Manual 15-01[1] is a greatly simplified approach to physiologically-based performance limits, based on ventilatory rates and gas density. Compared to older standards, the 2015 document allows testing laboratories to make maximum use of all of their testing data, and to present that data in an easily interpreted table.

Another way to use physiology to predict diver tolerance to UBA is to use the *Predict* risk assessment software developed at NEDU[5]. In fact, *Predict* is a more faithful application of the constant respiratory impedance concept than is the simplified tabular approach[1].

Predict is a very simple form of Probability Risk Assessment[6], and is useful in cases where the Navy wants to know the degree of <u>un</u>acceptability of a UBA. In other words, rather than NEDU simply saying a UBA is unacceptable, *Predict* can estimate the risk to diver and mission of using a particular UBA in a given diving scenario, based on past diving experience.

The most recent description of the *Predict* software is found in NEDU Technical Report 15-03, 2015[5]. Some of that description is repeated here, but the primary goal of this report is to provide an example of where probabilistic risk prediction is most useful.

BACKGROUND

Table 4-13 of NEDU's latest unmanned testing manual[1] shows how test data on a MK 21 diving helmet is displayed in a two-dimensional format, tabulating resistive effort (RE) as a function of diving depth and respiratory minute ventilation (RMV). That data is compared to **goals**, relating to diver comfort, and **limits** relating to diver tolerance. The outcome of the comparison with goals and limits is shown by color coding, as explained in the legend to Table 1 below.

Table 1. Resistive Effort (RE) in kPa for MK 21 Mod 1 Helmets with Air.

RMV (L/min)	Depth (fsw)							Goals (kPa)
	0	33	66	99	132	165	198	
22.5	--	0.49	0.54	0.65	0.55	0.58	0.62	1.37
40.0	--	0.59	0.67	0.82	0.78	0.84	0.91	1.37
62.5	--	0.67	0.88	1.14	1.17	1.32	1.63	1.54
75.0	--	0.74	1.05	1.35	1.40	1.82	2.17	2.16
90.0	--	0.85	1.24	1.68	1.92	~~2.34~~	~~2.60~~	---
Limits (kPa)	2.99	2.78	2.57	2.36	2.15	1.94	1.79	

Data from NEDU TR 11-93[7]. RMV = Respiratory Minute Volume
Green (bold): RE met both limits and goals.
Grey: Statistically, RE met limits or goals but not both.
Red (strikethrough): RE met neither limits nor goals.

Usually, a UBA evaluated at NEDU is suitable for most diving depths, as shown in Table 1. However, one instance where that was not the case is shown below in Table 2. For simplicity, only the resistive effort data for one ventilation rate (RMV, respiratory minute volume) is shown; 62.5 L/min. In accordance with the color codes from Table 1, there was only one depth (33 fsw, indicated by gray font) where the UBA met the **limits** on resistive effort (in kPa), even though it exceeded the **goal** for an RMV of 62.5 L/min.

Table 2. Resistive Effort in kPa for an Unspecified Helmet with Air

RMV (L/min)	Depth (fsw)							Goals (kPa)
	0	33	66	99	132	165	198	
62.5		2.71	~~3.49~~	~~3.80~~	~~4.17~~	~~4.73~~	~~5.04~~	1.54
Limits (kPa)	2.99	2.78	2.57	2.36	2.15	1.94	1.79	

By definition, limits are absolute. But in the case where a UBA does not meet any worthwhile diving depth, the following question might be asked: *What is the probability that a diver will encounter breathing difficulty at 66 fsw, or 99 fsw?*

Normally that question would be irrelevant: the Navy does not dive marginal diving gear. However, if that equipment had a unique capability not found in other types of UBA, for

instance, providing diver protection from toxic environments, then the above question will inevitably be asked.

The tabular approach in Tables 1 and 2 cannot answer that question. However, *Predict* software allows the prediction of the probability of an "untoward event" such as loss of consciousness or breathlessness (dyspnea) resulting in cessation of work. Unlike the "limits" approach which is based on diver data obtained at the State University of New York at Buffalo[8,9], the "predictions" are based on physiological data obtained from Navy dives conducted at NEDU and the Naval Medical Research Institute (NMRI).

METHODS

Predict software needs only two parameters to calculate the probability of an untoward event. Those parameters are gas density (ρ) which varies with depth and gas mixture, and experimentally determined peak to peak mouth pressure (ΔPm) which varies with RMV and equipment breathing resistance. Those parameters are then applied to prediction equations developed from maximum likelihood analyses of NMRI and NEDU human performance data[10,11].

Peak to Peak Pressure and Resistive Effort

In at least one NEDU report, unmanned testing results have been expressed in terms of breathing resistance with units of $cmH_2O/L/s$, or $kPa/(L/s)$[12]. Respiratory resistance is physically analogous to electrical resistance which has units of volts/(coulombs/s).

Just as the units of electrical resistance are conventionally simplified to "ohms" (Ω), respiratory resistance is likewise simplified. However, unlike the electrical case, in diving applications it is simplified by transformation[14]. That transformation comes from dividing true flow resistance by tidal volume. The result has sometimes been misnamed "Work of Breathing", but strangely without units of work. Instead, it has units of pressure. Reflecting the fact that people can immediately sense respiratory pressure but not work, NEDU has used the term "effort", or more exactly, "resistive effort," ever since the publication of the 1994 NEDU unmanned testing manual[3]. The term "effort" has since been used in at least one medical physiology textbook covering respiratory mechanics[14].

Resistive effort (RE), or volume-weighted average respiratory pressure, is commonly reported in NEDU reports and the past two NEDU unmanned testing technical manuals[1,3]. Nevertheless, *Predict* uses another type of pressure, peak-to-peak mouth pressure because the *Predict* model was calibrated by peak-to-peak mouth pressure measured in manned dives. RE *per se* cannot currently be measured in manned dives due to the lack of accurate measurements of lung volume data in immersed working divers.

Data Entry

Predict software converts depth and gas mixture to gas density at 37°C, the assumed

average temperature within the alveolar region of a diver's lungs. For instance, for an air dive to 198 fsw, *Predict* shows that depth is 60.7 msw and absolute pressure is 7 atmospheres. Gas density is 8 g/L at 37°C, or 0.52 lb per cubic foot at 70°F.

For mixed gas, the amount of oxygen in the mixture can be entered either as a percentage or partial pressure. The diluent is user selectable as either nitrogen or helium.

The final data entered into the *Predict* software is peak-to-peak mouth pressure (ΔPm). (Table 3). That example table provides peak inspiratory and peak expiratory pressure for an ensemble of ten pressure-volume breathing loops for each depth and water temperature.

ΔPm for the test results in Table 3 was $2.086 + 6.75$ kPa = 8.84 kPa, or 90.2 cmH$_2$O. (To convert from kPa units of pressure to cmH$_2$O, as required by *Predict*, multiply by approximately 10.2.)

Table 3. Example test summary for a single testing run at 198 fsw, air breathing medium

RMV	62.5	liters/minute
Average Depth	198	fsw
Ens. Average Peak Inhale Pressure	-2.086	kPa
Ens. Average Peak Exhale Pressure	6.75	kPa
Average Supply Pressure	244.7	psi
Max Supply Pressure	249.2	psi
Min Supply Pressure	240.3	psi
Average Overbottom Pressure	142.5	psi
Max Overbottom Pressure	160.5	psi
Min Overbottom Pressure	111.5	psi
Offset Pressure	-3.238	kPa
Binned Ensemble Averaged Resistive Effort	5.373	kPa
Inhale Ensemble Averaged Resistive Effort	2.932	kPa
Exhale Ensemble Averaged Resistive Effort	2.441	kPa

A full test on five diving helmets includes 7 tests per helmet for a helmet tested to seven atmospheres (198 fsw) or ten tests if tested to 297 fsw, assuming RE is measured at one atmosphere increments starting at the surface (1 atm). A total of 35 to 50 measurements are therefore typical for such testing, depending on maximum depth.

RESULTS

Probability Estimation

For the example of Table 3, *Predict* found that a ΔPm of 90.2 cmH$_2$O yielded a probability of an untoward event of 0.95. That result is interpreted as follows: if a diver breathing air were to generate a 90.2 cmH$_2$O peak to peak mouth pressure at 198 fsw, and sustain that for an approximately six minute period[†], there is a 95% probability that the diver would be

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[†] The NEDU protocols upon which much of the dive failure data was gathered used alternating work/rest scenarios (6 min work/4 minutes rest), at incrementing workloads. NMRI data was based on prolonged steady work[10].

forced to quit working due to breathlessness or loss of consciousness.

For further examples, data in the format of Table 2 was compiled on two new helmet systems (labeled H1 and H5). ΔPm for each helmet was found as shown in Table 3. In Figures 2 and 3, spline lines connect the peak to peak pressures and predicted event probabilities, respectively, for each helmet. However, those splines do not imply a smooth function between plotted data points.
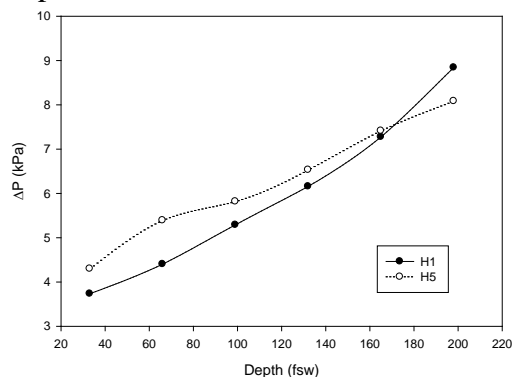

Figure 2. ΔPm as a function of depth at an RMV of 62.5 L/min
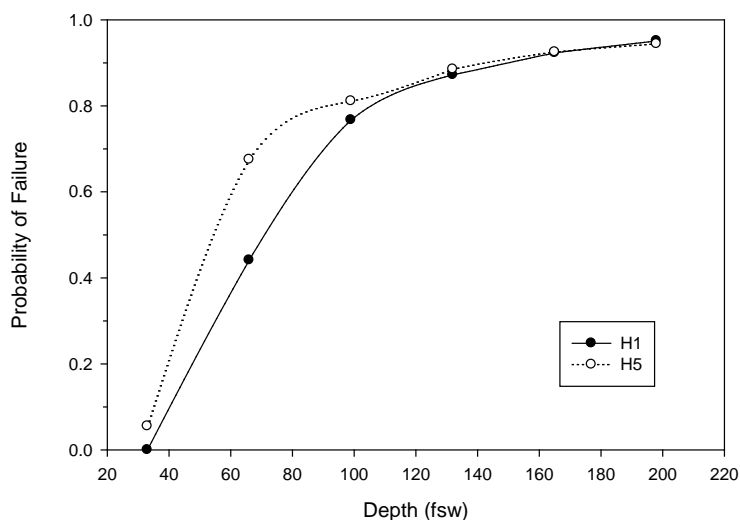
Figure 3. Probability of dive failure as a function of depth.

DISCUSSION

For the data set used to derive the *Predict* equation parameters (Appendix D), the equations relating probability of an event to dive depth best fit the Hill equation, a sigmoidal dose-response curve as routinely found in pharmacology. In biology, saturation of blood plasma, red blood cells or cellular binding sites is an expected outcome of increasing dosage of oxygen or drugs. Saturation is key to most processes described by the Hill equation.

However, when dealing with the probabilities of a physiological event, the saturation explanation is not necessarily applicable. A 2009 review of the Hill equation discussed the fitting of parameters by probabilistic statistical methods such as maximum likelihood[15,16]. Of particular relevance to this discussion is the use of probabilistic modeling for studies of decompression sickness incidence[17] as well as drug induced nephrotoxicity[18]. In these cases, the highest probability of an event is associated not with saturation but with organ or organism death.

The maximum likelihood analysis of NEDU and NMRI diving data revealed that for a given gas density, the probability of an untoward event was higher in a helium (He) environment than in a nitrogen (N_2) environment (Figure 4). This could be due to the effect of high pressure, as suggested in a description of NEDU's 1800 fsw (55.5 ata) dive[12]. For a given density, heliox must be at a greater pressure than nitrox. Alternatively, at high densities of a nitrogen atmosphere, nitrogen narcosis might blunt the perception of breathlessness or "dyspnea", to use the medical terminology.

The difference between probabilities for He and N_2 was statistically significant[10]. Predictably, at low gas densities there was considerable overlap in the confidence regions for the best fit predictions. That is not surprising since at low densities, neither narcosis nor high pressure effects would be expected.
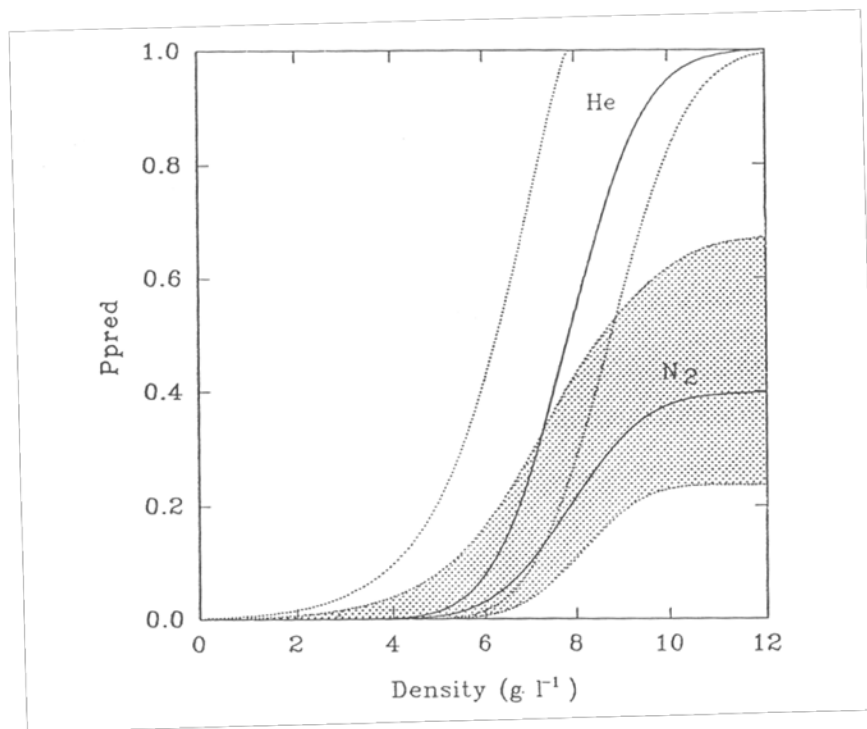

Figure 4. Best fit and confidence intervals for Hill equations applied to dive data. ΔPm = 15 cmH₂O.

For reference, the density of air at 37°C and 140 fsw is calculated by *Predict* to be 6 g/L, as is a helium-oxygen mixture (heliox) at 1125 fsw with a PO_2 of 0.45 atmospheres. The gas density of air at the same temperature and 200 fsw is calculated as 8 g/L.

Predict uses the best estimates for its predictions. Those best estimates are shown as the solid lines in the middle of the He and N_2 confidence regions in Figure 4 for a ΔPm of 15 cmH$_2$O. For a gas density of 8 g/L those best estimates range from a probability of 0.22 to 0.6.

Considering the uncertainty of the resulting predictions, including the width of the 95% confidence intervals, the following can be said: at 8 g/L, the probability of an eventful dive ranges from 0.10 to 1.0. That is not particularly illuminating, and points out the benefit of finding and using the best estimate of the existing data. That said, of the two best estimates, 0.22 to 0.6, the lower estimate assumes that nitrogen narcosis or the lack of a high pressure effect (such as HPNS) is moderating diver risk.

In the case of a diving helmet at 198 fsw, the supposition of an HPNS-like effect is not reasonable, whereas narcosis arguably is reasonable. Nevertheless, the higher probability estimate is always going to be conservative. It reveals the highest risk, and therefore offers the greatest benefit to the diver.

To always calculate the highest risk upon initiation of the *Predict* program, check the checkbox labeled "no narcosis". Conversely, to estimate the lower risk, uncheck the box. It is unchecked by default.

CONCLUSIONS

The *Predict* software and analysis technique reveals that in the case of the two example diving helmets (H1 and H5), the probability of a diver experiencing an untoward event at 33 fsw, while performing heavy work, is essentially zero. That result agrees with the limit-based approach described in reference (1), and shown in Table 2.

Above 33 fsw, the limit-based approach of Table 2 simply shows that the limit is **not met**. *Predict* augments that conclusion by estimating that at 66 fsw, the probability of an untoward event rises to 0.50 and above, and at 99 fsw the best estimate of the event probability is about 0.80. In other words, it would be unwise to dive helmets H1 and H5 at 66 fsw, and foolhardy to dive them at 99 fsw.

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Appendix A. *Predict* Software

Predict uses parameters fit with maximum likelihood statistical techniques to NEDU and the Naval Medical Research Institute (NMRI) data, to derive a probabilistic estimation of risk for high work load dives. As such, respiratory flow rate is not implicitly involved. The following equations apply:

$$Dose = \Delta P + (a \cdot \rho) - b \qquad (1)$$

where Dose is a respiratory loading "dose", ΔP is peak to peak mouth pressure, and a and b are constants representing a slope and threshold. Gas density is ρ in units of g/L. The probability of an "event" is modeled by the Hill equation, and takes the form of:

$$P_e = \left[\frac{1}{1 + \dfrac{d50^c}{dose^c}} \right] \qquad (2)$$

where d50 is the dose that results in a 50% dive failure rate, and c is a constant, fit to the data by maximum likelihood techniques.
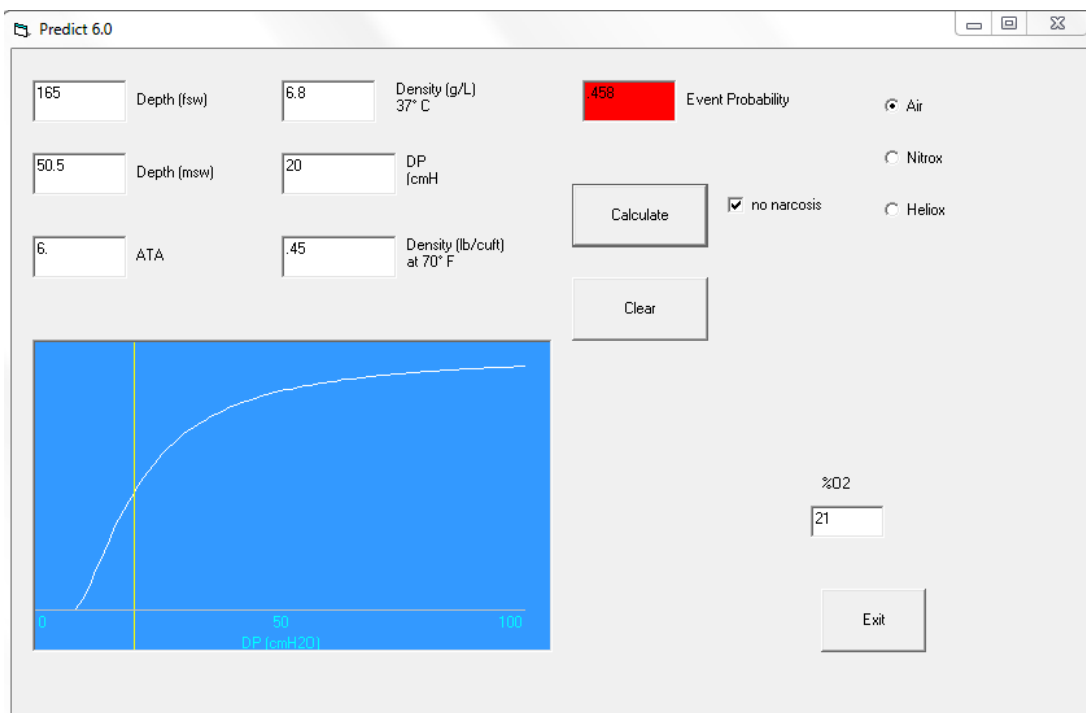

Figure A-1. Screen shot from *Predict*, dive failure estimation software. An air dive to 165 fsw, with a peak-to-peak mouth pressure of 20 cmH₂O. The estimated risk of an event is almost 46%.
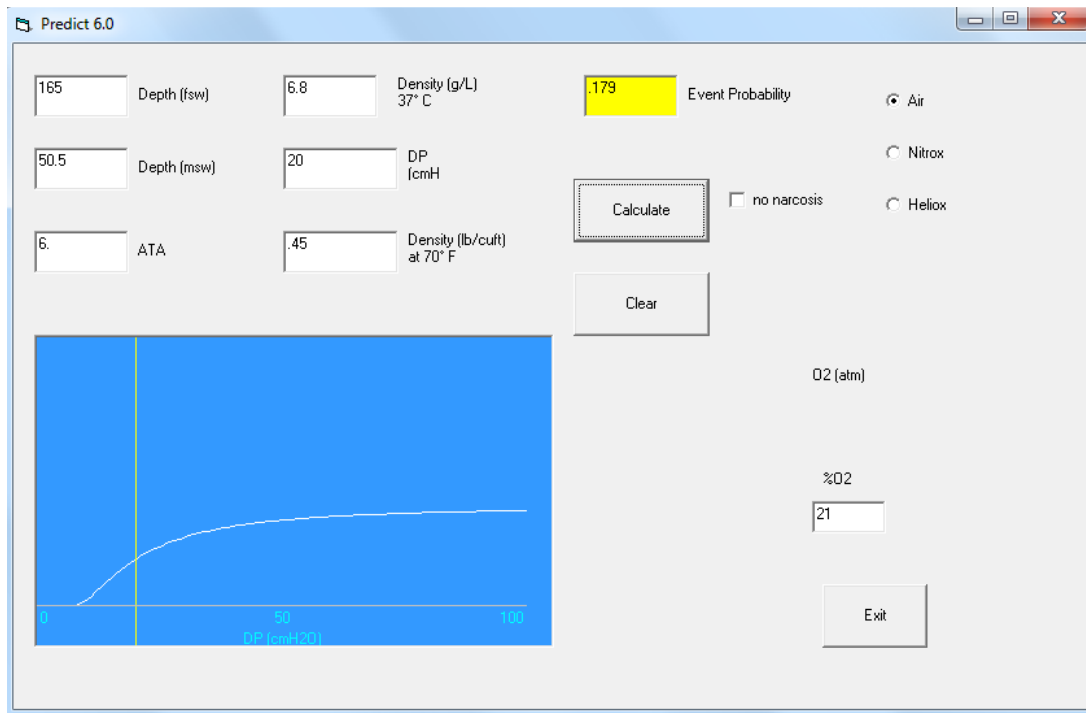
Figure A-**2**. The same analysis as in Figure 1, except the potential narcotic effect of air at 165 fsw influenced the failure probability estimate. The estimated risk of an event is lowered to 18%. This hypothesized narcosis effect comes from the data published in Clarke (1992)[10].
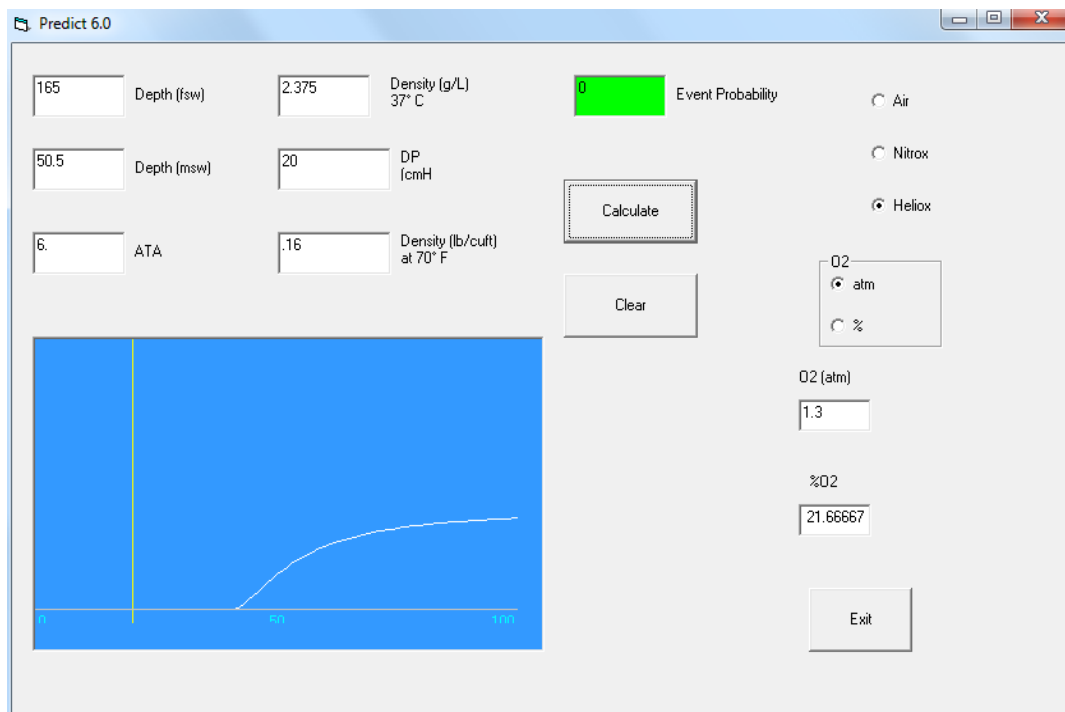

Figure A-3. A heliox dive to 165 fsw, with a peak-to-peak mouth pressure of 20 cmH$_2$O. The estimated risk of an event is zero.
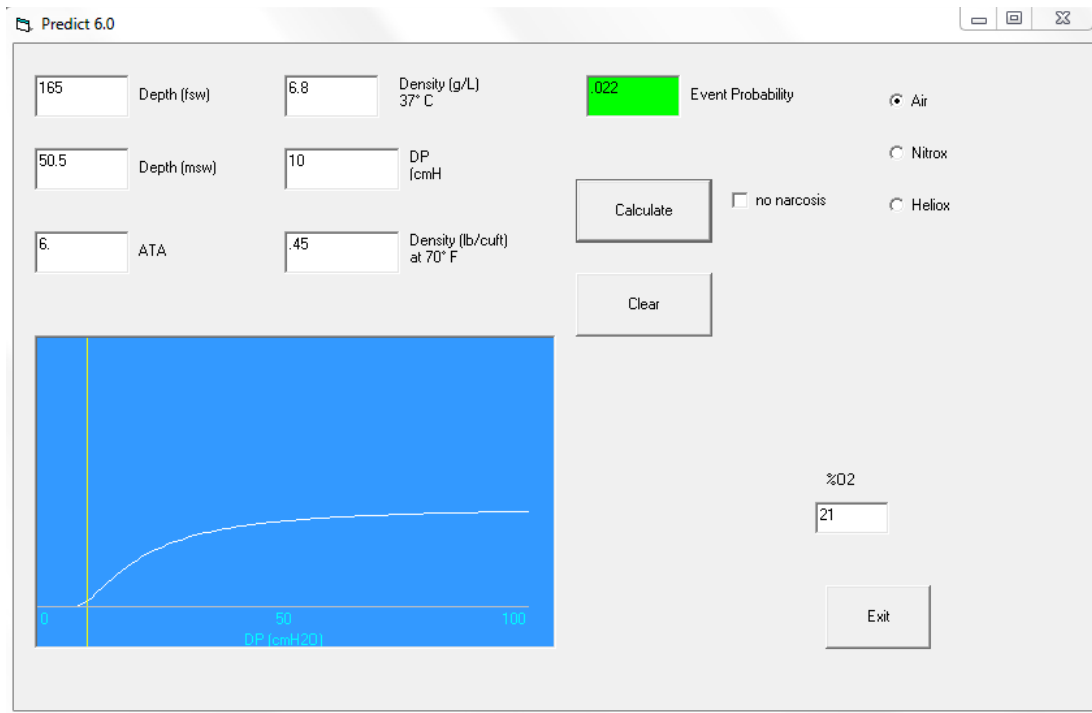
Figure A-4. An air dive to 165 fsw, with a peak-to-peak mouth pressure of 10 cmH$_2$O. By halving the workload and the peak-to-peak mouth pressure, the estimated risk of an eventful dive is reduced from 18% (Figure A-2) to 2%.

Appendix B. The Effect of Gas Density

The material in this appendix is largely reprinted from NEDU TR 15-03.

The effect of elevated gas density on respiratory resistance, especially in divers during deep saturation dives, has been one of the most extensively investigated subjects funded by the US and French Navies. Examples of these seminal studies are found in Anthonisen et al (1971), Broussolle et al (1976), Maio and Farhi (1967), Peterson and Wright (1976), and Varene et al (1967).

Clarke et al (1982) found on a 457 msw (1500 fsw) dive at NEDU that the power for respiratory resistance as a function of gas density in six resting subjects (over 120 measurements) was,

$$R_{int} = a \cdot \rho^{0.42}$$

where R_{int} was respiratory resistance measured by the interrupter technique (Neergarrd and Wirtz, 1927; Child 2005). R_{int} estimates the ratio of alveolar pressure and respiratory flow at the moment of flow interruption. Therefore the pressure drop across the saturation diver's respiratory system at rest was on average,

$$\Delta P = a \cdot \rho^{0.42} \cdot \dot{V}$$

The power of ρ across the six divers ranged from 0.36 to 0.50, not much different from the 0.5 used in the first term of Pedley's fluid dynamic based theory,

$$\Delta P_V = K_3 \cdot (\mu \cdot \rho)^{\frac{1}{2}} \cdot \dot{V}^{\frac{3}{2}} + K_4 \cdot \rho \cdot \dot{V}^2$$

and was similar to the results of Jaeger and Matthys (1970) for density changes at 1 ata.

At low flow rates, ΔP is relatively insensitive to density changes. That is not at all surprising since low flow rates encourage laminar flow, which has long been known to be density independent. Flow in the human airways is "conditional", lying somewhere between laminar and fully turbulent flow depending on location within the airways and conditions of density and flow rate. Nevertheless, low flow rates act to minimize density dependence.

Interestingly, it's been shown that there is a statistical difference between the probability of an eventful dive when the same gas density is achieved in a nitrogen environment versus a helium environment (Clarke, 1992). The nitrogen background is associated with a better outcome. That result remains unexplained, but may allude to a salutatory effect of nitrogen narcosis. Speculatively, light to mild narcosis may improve diver comfort and ameliorate the sensation of dyspnea. Whether that speculation is in fact true or not awaits further research.

Thalmann and Piantadosi (1981) suggest that the alternative explanation is that high pressure itself contributes to the sensation of dyspnea since episodic "work rates in excess of 250 watts can be done at gas densities of 8 g/L on air before dyspnea becomes intolerable" whereas at 7.8 g/L (47 ata) divers could just complete 150 watts of exercise. At 55.5 ata (~9.1 g/L) divers could only complete 100 watts.

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Appendix C: The mathematics behind *Predict* software

Below is a MathCad (Mathsoft Inc., Cambridge, MA) interpretation of the mathematics behind the *Predict* software used by NEDU to estimate the nonlinear correlation between mouth pressure and gas density with the probability of an untoward event; an eventful dive.

Predict expresses peak to peak mouth pressure and gas density as contributors to respiratory loading. The amount of that loading is summed as a "dose". Dose is then inserted into the Hill equation to predict the probability of a diver encountering difficulty of respiratory origin during a moderately strenuous dive.

The parameters used in both *Predict* and its MathCad implementation come from the maximum likelihood fitting of binary dive outcomes (eventful or uneventful) for instrumented bounce and saturation Navy dives at depths to 450 msw.

Parameters and variables are as follows:

Pf – probability of an eventful dive, dive failure; DP – ΔP or peak to peak mouth pressure; slpe – slope of the allowed DP vs gas density relationship, thr – threshold of dose required to be exceeded before respiratory difficulties begin occurring. D50 is the dose that causes an estimated 50% dive failure rate, pwr or n – the power used in the Hill equation; density is gas density at depth and at body temperature (37°C).

Predict_TR2013.mcd

Five parameters came from the maximum likelihood fitting of data from NEDU and NMRI, at depths to 457 msw, 1500 feet.

$$slpe := 7.4454 \qquad thr := 58.579 \qquad d50 := 13.675 \qquad pwr := 1.5664 \qquad del := -0.6102$$

$$n := pwr \qquad n = 1.566$$

Peak to peak pressure and gas density (at 37°C) come from the experimental conditions and measurements to be evaluated.

$DP = \Delta P$. Units of DP are cm_H_2O. 1 kPa ~ 10 cm_H_2O.

$$DP := 20 \quad cm\_H2O \qquad\qquad density := 6.8 \quad g/L$$

We will be establishing a dose-response curve like that for pharamecuticals. The "dose" is composed of DP and gas density.

$$Dose_0 := DP + slpe \cdot density \qquad Dose_0 = 70.629$$

$$Dose_1 := (DP + slpe \cdot density) - thr$$

If the dose is greater than the threshold dose (thr) then the threshold is subtracted from the calculated dose. If not, then the dose is set to zero.

$$Dose := \begin{vmatrix} 0 & if & Dose_0 \le thr \\ Dose_1 & otherwise \end{vmatrix}$$

$Dose = 12.05$ The calculated dose is for given DP and density.

$$Pf := \frac{Dose^n}{Dose^n + d50^n} \qquad\qquad Pf = 0.451 \qquad \text{From the Hill equation, the probability of failure is 0.45.}$$

For DPs ranging from 0 to 50 cm_H_2O:

$i := 0 .. 50$

$slpe = 7.445$

$density = 6.8$

$DP_i := i$

$Dose_i := DP_i + slpe \cdot density$

$Dose1_i := Dose_i - thr$

$+$

$$Dose2_i := \begin{vmatrix} 0 & if\ Dose_i \le thr \\ Dose1_i & otherwise \end{vmatrix}$$

$$Pf_i := \frac{\left(Dose2_i\right)^n}{\left(Dose2_i\right)^n + d50^n}$$

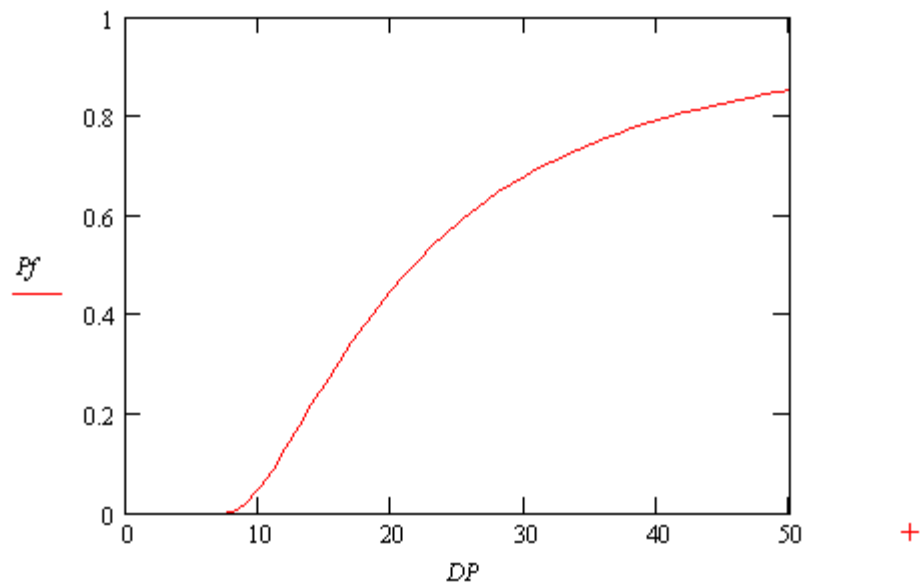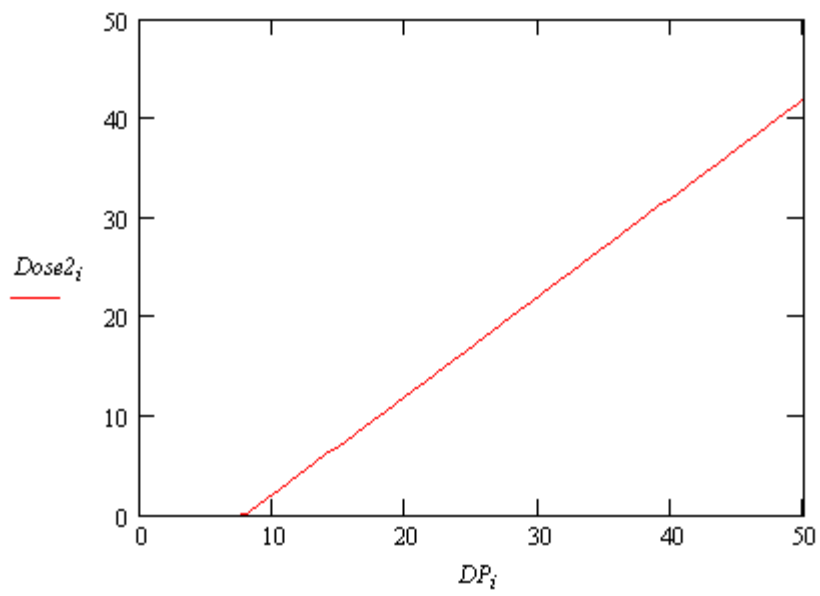| $DP_i =$	$Dose_i =$	$Dose1_i =$	$Dose2_i =$
0	50.629	-7.95	0
1	51.629	-6.95	0
2	52.629	-5.95	0
3	53.629	-4.95	0
4	54.629	-3.95	0
5	55.629	-2.95	0
6	56.629	-1.95	0
7	57.629	-0.95	0
8	58.629	0.05	0.05
9	59.629	1.05	1.05
10	60.629	2.05	2.05
11	61.629	3.05	3.05
12	62.629	4.05	4.05
13	63.629	5.05	5.05
14	64.629	6.05	6.05
15	65.629	7.05	7.05

$Dose1_{20} = 12.05$ $Dose2_{20} = 12.05$ *The dose becomes non-zero at 8 cmH_2O*

Like typical dose-response functions, the probability of dive failure rises monotonically and curvilinearly once dose crosses a threshold.

Appendix D: The data behind *Predict* risk assessment software

Each of the dots below represents a dive with moderately heavy exercise at a calculated gas density. ΔP is measured peak-to-peak mouth pressure. Numerous data points are superimposed on each other so not all the data is visible in this two-dimensional plot.

The diagonal solid black line shows the demarcation between uneventful dives (black-filled circles) and mostly eventful dives (red-filled circles). As ΔP rises above the zero risk line for any gas density, there is an increase in the probability of an eventful dive. Isoprobability lines are drawn for untoward event probabilities ranging from zero to 0.5.

As a gas density reference, air at 140 fsw and 37°C (average lung temperature) has a density of 6 g/L, as does a helium-oxygen mixture at 1125 fsw (with a PO_2 of 0.45 ata). For the same temperature, air at 200 fsw has a density of 8 g/L.

During NEDU's two deepest saturation dives, 1500 fsw (1977) and 1800 fsw (1979), *Predict* calculates a gas density at 37°F of 7.8 and 9.2 g/L, respectively. We can infer from this graph that the probability of an eventful hard working dive at 1800 fsw is very high, a fact which matched actual dive results[‡]. The event probability returned from running *Predict* for an 1800 fsw dive is 0.78.
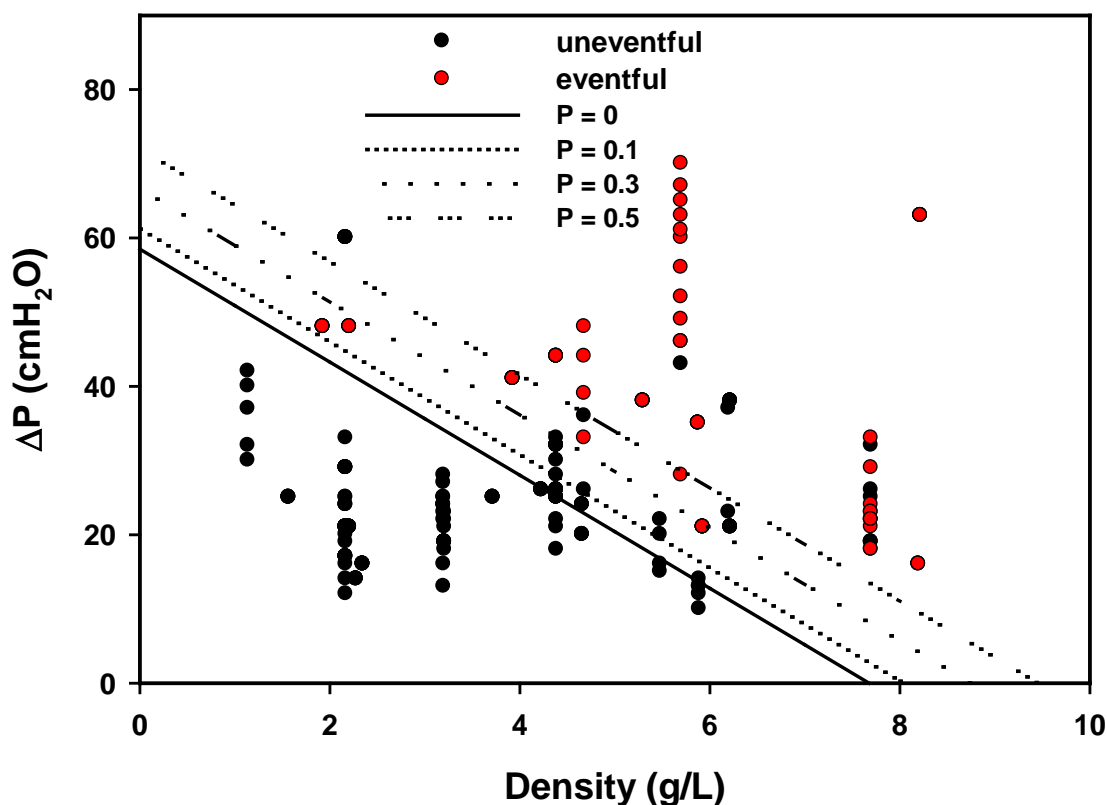
[‡] Thalmann, E.D., Piantadosi, C.A. Submerged exercise at pressure up to 55.5 ata. Abstract of the Undersea and Hyperbaric Medical Society, Annual Scientific Meeting, May 25-29, 1981.